

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings of claims in the application.

Listing of claims:

Claim 1 (withdrawn) A method for modulating lymphocyte activity, comprising contacting a BTLA-positive lymphocyte with a bioactive agent capable of modulating BTLA-mediated signaling in an amount effective to modulate at least one lymphocyte activity.

Claim 2 (withdrawn) The method according to claim 1, wherein said agent comprises an antagonist of BTLA-mediated signaling, and wherein said contacting inhibits the attenuation of lymphocyte activity mediated by BTLA signaling.

Claim 3 (withdrawn) The method according to claim 2, wherein said contacting increases lymphocyte activity.

Claim 4 (withdrawn) The method according to claim 2, wherein said antagonist comprises a blocking agent capable of interfering with the functional interaction of BTLA and B7x.

Claim 5 (withdrawn) The method according to claim 4, wherein said blocking agent comprises an anti-BTLA antibody capable of specifically binding to the extracellular domain of BTLA, wherein said binding interferes with the interaction of BTLA and B7x.

Claim 6 (withdrawn) The method according to claim 4, wherein said blocking agent comprises a soluble BTLA protein.

Claim 7 (withdrawn) The method according to claim 4, wherein said blocking agent comprises a soluble BTLA fusion protein.

Claim 8 (withdrawn) The method according to claim 4, wherein said blocking agent comprises an anti-B7x antibody capable of specifically binding to the extracellular domain of B7x, wherein said binding interferes with the interaction of BTLA and B7x.

Claim 9 (withdrawn) The method according to claim 4, wherein the blocking agent is selected from the group consisting of anti-BTLA antibodies, anti-B7x antibodies, BTLA polypeptides, BTLA fusion proteins, and small molecule chemical inhibitors of the interaction between BTLA and B7x.

Claim 10 (withdrawn) The method according to claim 1, wherein said bioactive agent comprises at least one antagonist selected from the group consisting of anti-BTLA antibodies, anti-B7x antibodies, soluble BTLA polypeptides, soluble BTLA fusion proteins, small molecule chemical inhibitors of BTLA-mediated signaling, BTLA antisense oligonucleotides, and B7x antisense oligonucleotides; and wherein said contacting increases lymphocyte activity.

Claim 11 (withdrawn) The method according to claim 1, wherein said agent comprises an agonist of BTLA-mediated signaling, and said contacting decreases lymphocyte activity.

Claim 12 (withdrawn) The method according to claim 11, wherein said agonist comprises a mimicking agent capable of mimicking the functional interaction of BTLA and B7x.

Claim 13 (withdrawn) The method according to claim 11, wherein said agonist comprises a mimicking agent capable of augmenting the functional interaction of BTLA and B7x.

Claim 14 (withdrawn) The method according to claim 12, wherein said mimicking agent comprises a soluble B7x protein capable of stimulating BTLA-4 mediated negative signaling, said B7x protein comprising the extracellular domain of B7x.

Claim 15 (withdrawn) The method according to claim 12, wherein said mimicking agent comprises a soluble B7x fusion protein capable of stimulating BTLA-4 mediated negative signaling, said B7x fusion protein comprising the extracellular domain of B7x.

Claim 16 (withdrawn) The method according to claim 11, wherein said agonist is selected from the group consisting of B7x proteins, B7x fusion proteins, small molecule chemical enhancers of BTLA-mediated signaling, and expression vectors comprising BTLA or B7x nucleic acids.

Claim 17 (withdrawn) The method according to claim 1, wherein said lymphocyte is a T lymphocyte and said lymphocyte activity is selected from the group consisting of activation, differentiation, proliferation, survival, cytolytic activity and cytokine production.

Claim 18 (withdrawn) The method according to claim 1, wherein said lymphocyte is a B lymphocyte and said lymphocyte activity is selected from the group consisting of activation, differentiation, proliferation, survival, and antibody production.

Claim 19 (withdrawn) The method according to claim 1, wherein said lymphocyte activity comprises a host immune response to a target antigen, said target antigen selected from the group consisting of a pathogen antigen, a vaccine antigen, and a tumor-associated antigen other than B7x.

Claim 20 (withdrawn) A method for modulating the interaction of a BTLA-positive lymphocyte with a B7x-positive cell, comprising contacting a BTLA-positive lymphocyte with a bioactive agent capable of modulating BTLA-mediated signaling in an amount effective to modulate at least one lymphocyte activity.

Claim 21 (withdrawn) The method according to claim 20, wherein said B7x-positive cell is a tumor cell and said bioactive agent comprises an antagonist of BTLA-mediated signaling, and wherein said contacting increases the host immune response against said tumor cell.

Claim 22 (withdrawn) The method according to claim 21, wherein said antagonist comprises a blocking agent capable of interfering with the functional interaction of BTLA and B7x.

Claim 23 (withdrawn) The method according to claim 22, wherein said blocking agent comprises an anti-BTLA antibody capable of specifically binding to the extracellular domain of BTLA, wherein said binding interferes with the interaction of BTLA and B7x.

Claim 24 (withdrawn) The method according to claim 22, wherein said blocking agent comprises a soluble BTLA protein.

Claim 25 (withdrawn) The method according to claim 22, wherein said blocking agent comprises a soluble BTLA fusion protein.

Claim 26 (withdrawn) The method according to claim 22, wherein said blocking agent comprises an anti-B7x antibody capable of specifically binding to the extracellular domain of B7x, wherein said binding interferes with the interaction of BTLA and B7x.

Claim 27 (withdrawn) The method according to claim 22, wherein the blocking agent is selected from the group consisting of anti-BTLA antibodies, anti-B7x antibodies, BTLA proteins, BTLA fusion proteins, and small molecule chemical inhibitors of the interaction between BTLA and B7x.

Claim 28 (withdrawn) The method according to claim 21, wherein said bioactive agent comprises at least one antagonist selected from the group consisting of anti-BTLA antibodies, anti-B7x antibodies, soluble BTLA proteins, soluble BTLA fusion proteins, small molecule chemical inhibitors of BTLA-mediated signaling, BTLA antisense oligonucleotides, B7x antisense oligonucleotides, and small RNA inhibitors; wherein said antagonists inhibit the attenuation of lymphocyte activity mediated by BTLA signaling.

Claim 29 (withdrawn) The method according to claim 20, wherein said B7x-positive cell comprises a non-tumor non-lymphoid host cell and said agent comprises an agonist of BTLA-mediated signaling, and wherein said contacting inhibits a host immune response against said non-lymphoid non-tumor host cell.

Claim 30 (withdrawn) The method according to claim 29, wherein said agonist comprises a mimicking agent capable of mimicking the functional interaction of BTLA and B7x.

Claim 31 (withdrawn) The method according to claim 29, wherein said agonist comprises a mimicking agent capable of augmenting the functional interaction of BTLA and B7x.

Claim 32 (withdrawn) The method according to claim 30, wherein said mimicking agent comprises a soluble B7x protein capable of stimulating BTLA mediated negative signaling, said B7x protein comprising the extracellular domain of B7x.

Claim 33 (withdrawn) The method according to claim 30, wherein said mimicking agent comprises a soluble B7x fusion protein capable of stimulating BTLA-4 mediated negative signaling, said B7x fusion protein comprising the extracellular domain of B7x.

Claim 34 (withdrawn) The method according to claim 30, wherein said agonist is selected from the group consisting of B7x proteins, B7x fusion proteins, small molecule chemical enhancers of BTLA-mediated signaling, and expression vectors comprising BTLA or B7x nucleic acids.

Claim 35 (withdrawn) A bioactive agent for modulating lymphocyte activity, wherein said bioactive agent comprises an antagonist of BTLA-mediated signaling which is capable of inhibiting the attenuation of lymphocyte activity mediated by BTLA signaling.

Claim 36 (withdrawn) The bioactive agent according to claim 35, wherein said modulation increases lymphocyte activity.

Claim 37 (withdrawn) The bioactive agent according to claim 35, wherein said antagonist comprises a blocking agent capable of interfering with the functional interaction of BTLA and B7x.

Claim 38 (withdrawn) The bioactive agent according to claim 37, wherein said blocking agent comprises an anti-BTLA antibody capable of specifically binding to the extracellular domain of BTLA, wherein said binding interferes with the functional interaction of BTLA and B7x.

Claim 39 (withdrawn) The bioactive agent according to claim 37, wherein said blocking agent comprises a soluble BTLA protein.

Claim 40 (withdrawn) The bioactive agent according to claim 37, wherein said blocking agent comprises a soluble BTLA fusion protein.

Claim 41 (withdrawn) The bioactive agent according to claim 37, wherein said blocking agent comprises an anti-B7x antibody capable of specifically binding to the extracellular domain of B7x, wherein said binding interferes with the functional interaction of BTLA and B7x.

Claim 42 (withdrawn) The bioactive agent according to claim 37, wherein said blocking agent is selected from the group consisting of anti-BTLA antibodies, anti-B7x antibodies, BTLA proteins, BTLA fusion proteins, and small molecular weight chemical inhibitors of the interaction between BTLA and B7x.

Claim 43 (withdrawn) The bioactive agent according to claim 35, wherein said bioactive agent comprises at least one antagonist selected from the group consisting of anti-BTLA antibodies, BTLA proteins, BTLA fusion proteins, small molecule chemical inhibitors of BTLA expression or BTLA-mediated signaling, BTLA antisense oligonucleotides, and small RNA inhibitors.

Claim 44 (withdrawn) A bioactive agent for modulating lymphocyte activity, wherein said bioactive agent comprises an agonist of BTLA-mediated signaling, and said modulation decreases lymphocyte activity.

Claim 45 (withdrawn) The bioactive agent according to claim 44, wherein said agonist comprises a mimicking agent capable of mimicking the functional interaction of BTLA and B7x.

Claim 46 (withdrawn) The bioactive agent according to claim 44, wherein said agonist comprises a mimicking agent capable of augmenting the functional interaction of BTLA and B7x.

Claim 47 (withdrawn) The bioactive agent according to claim 45, wherein said mimicking agent comprises a B7x protein capable of stimulating BTLA-4 mediated negative signaling, said B7x protein comprising the extracellular domain of B7x.

Claim 48 (withdrawn) The bioactive agent according to claim 45, wherein said mimicking agent comprises a B7x fusion protein capable of stimulating BTLA-4 mediated negative signaling, said B7x fusion protein comprising the extracellular domain of B7x.

Claim 49 (withdrawn) The bioactive agent according to claim 44, wherein said agonist is selected from the group consisting of B7x proteins, B7x fusion proteins, small molecule chemical enhancers of BTLA-mediated signaling, expression vectors comprising BTLA nucleic acids, and expression vectors comprising B7x nucleic acids.

Claim 50 (withdrawn) A method for treating cancer in a patient having B7x-positive tumor cells comprising administering to the patient an antagonist of BTLA-mediated signaling, wherein said administration is effective to increase the host immune response against said B7x-positive tumor cell.

Claim 51 (withdrawn) The method according to claim 50, wherein said antagonist comprises a blocking agent capable of interfering with the functional interaction of BTLA and B7x.

Claim 52 (withdrawn) The method according to claim 51, wherein said blocking agent comprises an anti-BTLA antibody capable of specifically binding to the extracellular domain of BTLA, wherein said binding interferes with the interaction of BTLA and B7x.

Claim 53 (withdrawn) The method according to claim 51, wherein said blocking agent comprises a soluble BTLA protein.

Claim 54 (withdrawn) The method according to claim 51, wherein said blocking agent comprises a soluble BTLA fusion protein.

Claim 55 (withdrawn) The method according to claim 51, wherein said blocking agent comprises an anti-B7x antibody capable of specifically binding to the extracellular domain of B7x, wherein said binding interferes with the interaction of BTLA and B7x.

Claim 56 (withdrawn) The method according to claim 51, wherein the blocking agent is selected from the group consisting of anti-BTLA antibodies, anti-B7x antibodies, BTLA proteins, BTLA fusion proteins, and small molecule chemical inhibitors of the interaction between BTLA and B7x.

Claim 57 (withdrawn) The method according to claim 50, wherein said bioactive agent comprises at least one antagonist selected from the group consisting of anti-BTLA antibodies, soluble BTLA proteins, soluble BTLA fusion proteins, small molecule chemical inhibitors of BTLA expression or BTLA-mediated signaling, BTLA antisense oligonucleotides, B7x antisense oligonucleotides, and small RNA inhibitors; wherein said antagonists inhibit the attenuation of lymphocyte activity mediated by BTLA signaling.

Claim 58 (withdrawn) A method for treating a patient having an autoimmune disease characterized by the presence of autoreactive BTLA-positive lymphocytes, comprising administering to the patient an agonist of BTLA-mediated signaling, wherein said administration is effective to inhibit an autoreactive immune response against non-lymphoid non-tumor host cells expressing B7x.

Claim 59 (withdrawn) The method according to claim 58, wherein said agonist comprises a mimicking agent capable of mimicking the functional interaction of BTLA and B7x.

Claim 60 (withdrawn) The method according to claim 58, wherein said agonist comprises a mimicking agent capable of augmenting the functional interaction of BTLA and B7x.

Claim 61 (withdrawn) The method according to claim 59, wherein said mimicking agent comprises a soluble B7x protein capable of stimulating BTLA mediated negative signaling, said B7x protein comprising the extracellular domain of B7x.

Claim 62 (withdrawn) The method according to claim 59, wherein said mimicking agent comprises a soluble B7x fusion protein capable of stimulating BTLA mediated negative signaling, said B7x fusion protein comprising the extracellular domain of B7x.

Claim 63 (withdrawn) The method according to claim 58, wherein said agonist is selected from the group consisting of B7x proteins, B7x fusion proteins, small molecule chemical enhancers of BTLA-mediated signaling, and expression vectors comprising BTLA or B7x nucleotides.

Claims 64-73 (cancelled)

Claim 74 (currently amended) An expression vector, comprising the recombinant BTLA nucleic acid according to ~~claim 64 or 73~~ any one of claims 91-94 operably linked to regulatory sequences recognizable by a host cell transfected with the recombinant BTLA nucleic acid.

Claim 75 (currently amended) A host cell, comprising the recombinant BTLA nucleic acid according to any one of claims 91-94 ~~claim 64 or 73~~.

Claim 76 (original) A host cell, comprising the expression vector of claim 74.

Claim 77 (original) A process for producing a BTLA protein, comprising culturing the host cell of claim 76 under conditions suitable for the expression of BTLA protein.

Claim 78 (original) The process of claim 77, further comprising isolating the BTLA protein.

Claim 79 (withdrawn) A BTLA protein produced by the process of claim 78.

Claim 80 (withdrawn) An isolated BTLA protein, comprising an amino acid sequence encoded by the recombinant BTLA nucleic acid of any of claims 64, 65, 69 and 70.

Claim 81 (withdrawn) An isolated BTLA protein, comprising an amino acid sequence having at least about 70% identity to the amino acid sequence set forth in SEQ ID NO:8 or 10.

Claim 82 (withdrawn) The isolated BTLA protein of claim 81, comprising an extracellular V-like Ig domain, a transmembrane region, and an intracellular domain of approximately 100 amino acids that comprises a Grb2 interaction site and two ITIM sequences.

Claim 83 (withdrawn) The isolated BTLA protein of claim 81, which is capable of interacting with B7x.

Claim 84 (withdrawn) The isolated BTLA protein of claim 81, which is capable of interacting with SHP-1, SHP-2, or both SHP-1 and SHP-2.

Claim 85 (withdrawn) The isolated BTLA protein of claim 81, which has BTLA signaling activity.

Claim 86 (withdrawn) The isolated BTLA protein of claim 81, which is capable of inhibiting lymphocyte activity.

Claim 87 (withdrawn) The isolated BTLA protein of claim 81, comprising the amino acid sequence set forth in SEQ ID NO:8 or 10.

Claim 88 (cancelled)

Claim 89 (cancelled)

Claim 90 (cancelled)

Claim 91 (currently amended) A recombinant BTLA nucleic acid according to claim 73, encoding a BTLA protein having at least about 95% identity to the amino acid sequence set forth in SEQ ID NO:8, wherein said BTLA protein comprises an extracellular V-like Ig domain, a transmembrane region, and an intracellular domain, and is capable of inducible association with SHP-2 in T cells.

Claim 92 (currently amended) [[A]] The recombinant BTLA nucleic acid according to claim [[73]] 91,
encoding a BTLA protein comprising the amino acid sequence set forth in ~~SEQ ID NO:6 or 8~~ SEQ ID
NO:8.

Claim 93 (new) The recombinant BTLA nucleic acid according to claim 91, encoding a BTLA protein
having at least about 98% identity to the amino acid sequence set forth in SEQ ID NO:8.

Claim 94 (new) The recombinant BTLA nucleic acid according to claim 91, wherein said nucleic acid
comprises the nucleotide sequence set forth in SEQ ID NO:7.